Requirement. Applicant reserves the right to prosecute cancelled claims and claims to non-elected inventions in subsequent applications.

Applicant respectfully requests entry of the present Amendment to facilitate prosecution and place the claims in condition for allowance.

After entry of the present amendment, claims 1, 4, 5, 7, 9, 10, 13, 16, 18-21, 23-29, 31-39, 53-56, 59, 98, 99, 102, 103, 117 and 119 are pending.

Support for Amendments

Support for the amendments above is found in the specification as discussed below. No new matter has been added.

Claim 115 has been cancelled and rewritten as new claim 119, in part due to the square brackets present in the claims. The use of these brackets is based on standard peptide nomenclature, as employed by those in the art. Accordingly, Claim 115 was re-written to avoid confusion regarding what has been amended in the claim, since 37 CFR § 1.121 requires the changes be shown by brackets. The following changes were made in re-writing claim 115 as new claim 119: (1) the letters followed by periods indicating claim elements in claim 115 were replaced by bracketed letters; (2) the semicolons objected to in the Office Action in part (b) of claim 115 were removed in claim 119; and (3) elements (l), (m), (n) and (o) of claim 115 were deleted in claim 119. Support for these changes is either self-evident (i.e., correction of typographical errors) or found in the specification, for example at page 43, line 4 – page 45, line 11.

Claim 1 was amended to provide antecedent basis for claim 119, by (1) reciting α-MSH, α -MSH analog and α -MSH agonist compounds, and (2) reciting α -MSH compounds selected from SEQ ID NO:1 or SEQ ID NO:2. Support for this amendment is found in the specification, for example at page 37, line 15 – page 38, line 26.

Claims 4, 5, 10, 55, 56 and 59 have been amended to recite α-MSH instead of MSH compounds. Support for this amendment is found in the specification, for example at page 37, line 22 – page 38, line 7.

Page 17 of the specification has been amended to correct typographical errors. Claim 117 has been amended to correct the claim dependency therein.

Objections

The claims stand objected to for certain informalities. Specifically, the Office Action objected to the recitation of letters followed by periods to identify certain claim elements of claim 115. Claim 115 has been cancelled and re-written as new claim 119, wherein said claim elements are indicated by letters in parentheses. Claim 115 was also objected to because of the recitation of certain semicolons in claim element (b); said semicolons have been changed to commas in new claim 119. In light of the instant amendments and remarks, Applicants respectfully submit that the basis for the objections to claim 115 in the Office Action has been obviated. Reconsideration and removal of the objections in the Office Action is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 4, 5, 7, 9, 10, 13, 16, 18-21, 23-29, 31-39, 53-56, 59, 98, 99, 102, 103 and 115 stand rejected as being indefinite under 35 U.S.C. § 112, second paragraph for various reasons.

Claim 1 was rejected for failing to provide antecedent basis for the recitation of certain α-MSH compounds in claim 115, and for the recitation of "said compound is administered" at line 5. Claim 1 has been amended to recite "α-MSH, α-MSH analog and an α-MSH agonist" and to recite "therapeutic composition" instead of "said compound." Without conceding the validity of this rejection, these changes were made in accordance with the suggestion in the Office Action at page 3.

Claim 4 was rejected for reciting allegedly confusing subject matter, and for reciting MSH instead of "α-MSH". To facilitate prosecution, and without conceding the validity of this rejection, Applicants have amended claim 4 to comply with the suggestion in the Office Action at page 3 by deleting "a peptide mimetic... agonist activity" at lines 3-5 and changing "MSH" to"α-MSH".

Claim 5 was rejected for reciting non-elected subject matter. To facilitate prosecution, Applicants have amended claim 5 to comply with the suggestion in the Office Action at page 3 by deleting " -MSH and -MSH".

Claim 115 was rejected for several reasons. First, the Office Action requested clarification of the relationship between the (1) the recitation of "the cyclized portion of the

compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system (CNS)" in element (o) of claim 115 and (2) "administration of said compound minimizes delivery of said compound to the [CNS]" in claim 1. Office Action at pages 3-4. In re-writing cancelled claim 15 as new claim 119, Applicants have deleted the α-MSH antagonists recited in elements (l), (m), (n) and (o) of claim 115 as being drawn to non-elected subject matter pertaining to, for example, methods for *increasing* body weight (See, e.g., Specification at page 28, line 21- page 29, line 2; and page 34, lines 5-20). The α-MSH antagonists of elements (l)-(o) of claim 115 (See, e.g., Specification at page 45, line 12 – page 47, line 15), while claim 119 (dependant on claim 1) is drawn to a method to *decrease* body weight or reducing the rate of weight gain in an animal.

Claim 9 was rejected for recitation of "MSH" instead of "α-MSH." Applicants cannot locate any recitation of "MSH" in claim 9, but have amended the claims to comply with the suggestion in the Office Action so as to clarify the invention being claimed.

Claims 1, 4, 5, 115 and "all other claims reciting 'α-MSH'" were rejected for lacking clear antecedent basis as to which "α-MSH" are being referred to. Without conceding the validity of this rejection, Applicants have chosen to amend Claim 1 to recite "a-MSH" as being selected from a Markush group of SEQ ID NO:1 and SEQ ID NO:2, so as to facilitate prosecution. Applicant reserves the right to prosecute non-elected subject matter in subsequent applications. Claims 4, 5 and new 119 (which re-writes cancelled claim 115) incorporate this claim limitation as these claims are dependent on claim 1 as amended. Accordingly, the Applicants respectfully submit that the basis for this rejection has been obviated.

The typographic error "a MSH" has been amended to "α-MSH" in accordance with the suggestion in the Office Action at page 3.

Applicants respectfully submit that these changes have obviated the basis for these rejections.

Conclusion

Reconsideration and allowance of the pending claims in light of the amendments and remarks above is respectfully requested. Applicants respectfully submit that the present Amendment and Response places the pending claims in condition for allowance.

Respectfully Submitted,

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APPENDIX: Complete Listing of Pending Claims (37 CFR § 1.121)
Marked to Show Present Amendments

1. (Twice Amended) A method to decrease the body weight or reduce the rate of weight gain in an animal, comprising administering to said animal a therapeutic composition comprising a melanocyte stimulating hormone (MSH) compound selected from the group consisting of α-MSH, α -MSH analog and an α-MSH agonist, wherein said [compound]therapeutic composition is administered to the periphery of said animal in an amount effective to measurably decrease body weight or reduce the rate of eight gain in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal, wherein said α-MSH is a peptide comprising an amino acid selected from the group consisting of the sequences represented by SEQ ID NO:1 and SEQ ID NO:2.

4. (Twice Amended) The method of Claim 1, wherein said compound is selected from the group consisting of α-melanocyte stimulating hormone (α-MSH), a biologically active fragment of α-MSH, a homologue of α-MSH having α-MSH agonist, activity, [a peptide mimetic of MSH having MSH agonist activity,]a non peptide mimetic of α-MSH having α-MSH agonist activity, and a fusion protein comprising an α-MSH protein or a biologically active fragment thereof.

5. (Once Amended) The method of Claim 1, wherein said compound is [selected from the group consisting of] α-MSH[, β-MSH and γ-MSH].

7. (Reiterated) The method of Claim 1, wherein said compound is an analog of a peptide having an amino acid sequence represented herein by SEQ ID NO:2.

9. (Once Amended) The method of Claim 1, wherein said compound is a peptide comprising an amino acid sequence represented by SEQ ID NO:1.

10. (Twice Amended) The method of Claim 1, wherein said α-MSH compound has the following identifying characteristics: (1) an ability to bind to a

melanocortin receptor that is expressed in peripheral tissues, and, (2) a biological activity selected from the group consisting of Stimulation of lipolysis and inhibition of the uptake of fatty acids by adipocytes.

13. (Once Amended) The method of Claim 1, wherein said Compound binds to a melanocortin receptor expressed in the peripheral tissues with a higher affinity than to melanocortin-4 receptors (MC4-R).

16. (Reiterated) The method of Claim 1, wherein said compound does not bind to MC4-R under physiological conditions.

18. (Reiterated) The method of Claim 1, wherein said compound does not activate MC4-R Linder physiological conditions.

19. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered transdermally.

20. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered topically.

21. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered parenterally.

23. (Reiterated) The method of Claim 1, wherein said therapeutic composition is administered in a controlled release formulation.

24. (Reiterated) The method of Claim 1, whereby administration of said compound is insufficient to cause a statistically significant change in the appetite of said animal as compared to before administration of said compound.

25. (Once Amended) The method of Claim 1, wherein said composition is administered in a dose of from about 0.1 μg to about 10 mg per kg body weight of said animal.

26. (Once Amended) The method of Claim 1, wherein said compound is administered in a dose of from about 1 μg to about 10 mg per kg body weight of said animal.

27. (Once Amended) The method of Claim 1, wherein said compound is administered in a dose of from about 40 μg to about 1 mg per kg body weight of said animal.

28. (Once Amended) The method of Claim 1, wherein said compound is from about 0.1% to about 90% of said therapeutic composition by weight.

29. (Once Amended) The method of Claim 1, wherein said Compound is from about 0.1% to about 1% of said therapeutic composition by weight.

31. (Once Amended) The method of Claim 1, wherein said decrease in body weight in said animal cart be measured within at least about one week of said step of administering said compound.

32. (Once Amended) The method of Claim 1, wherein said animal has serum leptin levels between about 0 ng/ml and 50 ng/ml prior to said step of administration.

33. (Once Amended) The method of Claim 1, wherein said animal has serum MSH levels between about 0 ng/ml and 10 ng/ml prior to said step of administration.

34. (Once Amended) The method of Claim 1, wherein said animal has a ratio of serum MSH levels to serum leptin levels of greater than about 1:100 prior to said step of administration.

35. (Once Amended) The method of Claim 1, wherein said animal is a human having a body mass index (BMI) of greater than 27 kilograms per square meter prior to administration of said compound.

36. (Once Amended) The method of Claim 1, wherein said composition further comprises another body weight regulating agent.

37. (Once Amended) The method of Claim 36, wherein said another body weight regulating agent is leptin.

38. (Once Amended) The method of Claim 37, wherein said composition comprises a ratio of said MSH compound to leptin of about 1:100.

39. (Once Amended) The method of Claim 37, wherein said d leptin in a dose of from about 0.1 μpg to about 100 mg per kg body weight of said animal.

53. (Reiterated) The method of Claim 1, wherein said animal is a human.

54. (Reiterated) The method of Claim 1, wherein said composition further comprises an antagonist of MC4-R.

55. (Twice Amended) The method of Claim 1, wherein said composition further comprises an agent that inhibits binding of said α-MSH Compound to an MC4-R.

56. (Twice Amended) The method of Claim 1, wherein said composition further comprises an agent which inhibits said α-MSH Compound from entering the central nervous system of said animal.

59. (Twice Amended) A method of decreasing the body weight or reducing the rate of weight gain in an animal, comprising administering to an animal a melanocyte stimulating hormone (MSH) compound selected from the group consisting of α-MSH and an α-MSH agonist in an amount effective to bind to melanocortin receptors expressed by said animal in said animal's peripheral tissues, said effective amount:

(a) being insufficient to substantially change the appetite of said animal after said step of administering as compared to before said step of administering;

(b) being between about 0.1 μg and about 10 mg per kg, of body weight of said animal;

(c) being sufficient to affect a biological activity selected from the group consisting of:

(i) lipolysis; and,

(ii) uptake of fatty acids by adipocytes in said animal; and,

(d) being effective to measurably decrease the body weight or reduce the rate of weight gain of said animal after said compound has been administered to said animal.

98. (Once Amended) The method of Claim 1, wherein said animal is at risk for or suffering from an obesity associated disorder.

99. (Reiterated) The method of Claim 98, wherein said obesity associated disorder is selected from the group consisting of non insulin dependent diabetes mellitus, cardiovascular disease, cancer, hypertension, osteoarthritis, stroke, respiratory problems, and gall bladder disease.

102. (Once Amended) The method of Claim 1, wherein said animal is at risk of or suffering from undesired body weight which is a side effect resulting from administration of a pharmaceutical compound.

103. (Reiterated) The method of Claim 102, wherein said pharmaceutical compound is selected from the group consisting of valproic acid, lithium, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRI).

117. (Once Amended) The method of claim [115]119, wherein (k) AA^5 is α,γ-diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp and AA^{11} is α,β-diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α-aminoadipic acid, α-aminopimelic acid, Glu or Asp.

119. (New) The method of Claim 1, wherein said compound is an α-MSH analog selected from the group consisting of:

(a) Ac-[Cys^4, D-Phe^7, Cys^{10}] α-MSH, wherein said Cys residues are connected by a disulfide bond;

(b) Ac-[Nle^4, $X_{aa}{}^5$, His^6, $X_{aa}{}^7$, Arg^8, Trp^9, $X_{aa}{}^{10}$] NH_2, (SEQ ID NO:3)

wherein $X_{aa}{}^5$ is Glu or Asp, $X_{aa}{}^7$ is Phe or D-Phe and $X_{aa}{}^{10}$ is a dibasic amino acid, Lys, ornithine, 2,4-diaminobutyric acid, or 2,3 diaminopropionic acid (Dpr);

(c) Ac-[Cys^4, Cys^{10}]α-$MSH_{1-13}NH_2$;

(d) R_1-W-X-Y-Z-R_2,

wherein R_1 is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;

W is selected from the group consisting of -His- and -D-His-;

X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO_2)D-Phe^7-;

Y is selected from the group consisting of -Arg- and -D-Arg-;

Z is selected from the group consisting of -Trp- and -D-Trp-; and,

R_2 is selected from the group consisting of -NH_2, -Gly-NH_2, and -Gly-Lys-NH_2;

(e) Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH_2 (SEQ ID NO:4);

wherein M is selected from the group consisting of Met, Nle, and Cys;

(f) [Nle^4, D-Phe^7]-α-MSH;

(g) [Nle^4, D-Phe^7] -α-MSH_{4-10};

(h) [Nle^4, D-Phe^7] -α-MSH_{4-11};

(i) [Nle^4, D-Phe^7,D-Trp^9] -α-MSH_{4-11};

(j) [Nle^4, D-Phe^7] -α-MSH_{4-9}; and

(k) Ac-[Nle^4, AA^5, D-Phe^7, AA^{10}]-R_1 or Ac-[Nle^4, AA^5, D-Phe^7, AA^{11}]-R_2;

wherein AA^5 may be either a L-or D-amino acid having an omega amino or carboxyl group in the side chain;

wherein AA^{10} may be diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_1 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}H_2$; α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$;

wherein AA^{11} may be L- or D-amino acid having an omega amino or carboxyl group in the side chain;

wherein R_2 is the designation a $MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$.